

## REMARKS

Consideration of the Preliminary Amendment

A preliminary amendment was filed in this case on July 7, 2004. Receipt of that document by the USPTO was confirmed by return post-card. In addition, a copy of the preliminary amendment appears in the "Image File Wrapper" section of PAIRS, as accessed through the USPTO website.

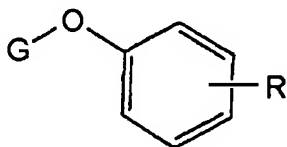
The preliminary amendment amended the claims to remove multiple dependencies and to add claims to certain subject matter that was eliminated from claims 2-4 due to the removal of those multiple dependencies. In addition, claim 1 was amended to remove the basis for the objection that later was stated in the June 1 office action.

A copy of the claims as amended in the preliminary amendment appears below for the examiner's convenience. PLEASE NOTE THAT NO FURTHER AMENDMENT TO THE CLAIMS IS BEING MADE IN THIS RESPONSE.

Consideration of the preliminary amendment is respectfully requested, as is entry of the amendments offered in that document. In order to facilitate further prosecution of this case, a substantive response to the office action is being provided in this paper

The claims as presented in the preliminary amendment read as follows:

1 (currently amended). A nanoscale self-aggregate comprising O-glycoside type oligolipid having a structure represented by the general formula (1) ~~shown below~~.



(1)

~~(In the formula, wherein~~ G represents an oligosaccharide radical composed of two to thirty monosaccharides, and R represents a hydrocarbon group containing six to twenty-five carbon atoms.)

2 (original). The nanoscale self-aggregate as in Claim 1 wherein the hydrocarbon group (R) is located in a meta position relative to the -O-G group in the general formula (1).

3 (currently amended). The nanoscale self-aggregate as in Claim 1 ~~or 2~~ wherein the oligosaccharide is a disaccharide.

4 (currently amended). The nanoscale self-aggregate as in Claim 1 ~~any one of Claims 1-3~~ wherein the oligosaccharide is lactose.

5 (new). The nanoscale self-aggregate as in Claim 2 wherein the oligosaccharide is a disaccharide.

6 (new). The nanoscale self-aggregate as in Claim 2 wherein the oligosaccharide is lactose.

7 (new). The nanoscale self-aggregate as in Claim 3 wherein the oligosaccharide is lactose.

8 (new). The nanoscale self-aggregate as in Claim 5 wherein the oligosaccharide is lactose.

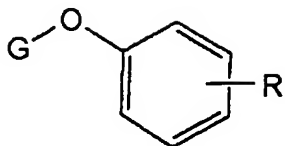
Regarding the objection to claim 1

This objection is moot, as the problem underlying this objection was dealt with in the claim amendments presented in the preliminary amendment.

Regarding the obviousness rejection

Original claims 1-4 stand rejected over a combination of references. Although those claims were amended in the preliminary amendment, their scope did not change (other than through the elimination of multiple dependencies). The rejection is respectfully traversed for the following reasons.

The present invention is a nanoscale self aggregate comprising a specific type of oligolipid. The oligolipid has the structure



. G is an oligosaccharide radical. R is a certain hydrocarbon group.

The John et al. *Advanced Materials* article appears to be the primary reference. The *Advanced Materials* article describes nanotubes formed from an oligolipid having a structure generally corresponding to that given above, except that G is a monosaccharide radical. These materials can be derived from cardanol, according to the reference. The *Advanced Materials* article does not describe or suggest that any type of oligosaccharide material could be substituted for the monosaccharide radical.

The *Advanced Materials* article does state “[w]e have previously demonstrated the remarkable effect of the headgroup conformation and chirality on the helical morphologies of nanofibers formed with peptide lipids”, noting the Shimizu et al. article that the Examiner now relies upon as a secondary reference. At least two points are significant here. First, the quoted statement follows a detailed discussion about how the cardanol-derived oligolipids appear to aggregate due to  $\pi$ - $\pi$  stacking of the phenyl groups, rather than via hydrogen bonding between sugar hydroxyls further stabilized by amide hydrogen bonding, as in polypeptide systems (like Shimizu’s). So, the cardanol-derived oligolipids are presented as acting in a fundamentally different manner than the peptide-based oligolipids. The second point is that, even in the peptide lipid systems (which, to underscore the point, operate in a different way), the impact of headgroup structure is said to have a “remarkable” effect.

The Shimizu article does not describe using oligomeric saccharides as headgroups, even in polypeptides. The Examiner misreads the first full paragraph of the second column of page 50 of the Shimizu article. What Shimizu is describing there is *not* the use of oligosaccharides in his polypeptide system. Instead, Shimizu is referring to the use of oligosaccharides in yet a *third* synthetic lipid system, and refers to the Hinz article as describing this.

Hinz’ synthetic lipid contains a mono- or oligosaccharide head group bonded through an ether linkage to a dialkylglycerol group. See the structures at page 5126 column 2. Hinz’ synthetic lipids lack the peptide structures of Shimizu’s materials, and lack the aromatic group of materials described in the *Advanced Materials* article (and those claimed in this application). The mechanism for self-aggregation by Hinz’ lipids must be different from those of the other

references, because Hinz' materials cannot engage in  $\pi$ - $\pi$  stacking (as they lack phenyl groups) or amide hydrogen bonding (as they lack nitrogen atoms).

Even in Hinz' systems, the structure of the head groups is said to have "dramatic" and "drastic" effects (see page 5134, second column, second full paragraph and page 5136, second column, immediately following the heading).

The only fair conclusion that can be reached from this combination of references is that there is a great degree of unpredictability associated with changes to the structures of synthetic lipids. Hinz concludes that for his particular lipids the size of the head group is a "dominating influence" on the structural organization of the lipid chains. But Hinz' lipids are far different than either Shimizu's or John's from a structural viewpoint, and the *Advanced Materials* article itself reports that cardanol-based lipids appear to operate by a unique mechanism (that cannot function in either Shimizu's or Hinz' lipids due to the lack of aromatic rings). The extent to which Hinz' statement can be said to be true for cardanol-based lipids cannot be ascertained or even predicted from the references. The scope of the effect cannot be predicted, either.

Accordingly, the current obviousness rejection cannot stand. Due to the significant differences in the structures of the lipids described in the cited references, the different mechanisms by which they self-aggregate, and the reference's explicit teachings that headgroup structure has enormous impact on the function of the lipids, it cannot be fairly said that it would have been obvious to substitute an oligosaccharide for the monosaccharides described in the *Advanced Materials* article with any reasonable expectation of success. The references clearly suggest that making a structural change of this type might be expected to profoundly change the function of the lipid. The references do not even allow one to predict whether the modified peptide would even retain the ability to self-aggregate at all, or if so, whether it would self-aggregate into a useful form.

The fourth reference relied on by the examiner is simply a background document describing polysaccharide chemistry. It does not relate to self-aggregating synthetic lipids.

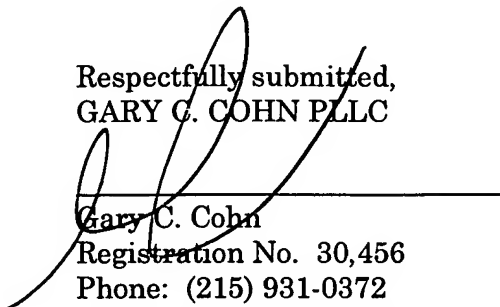
### Conclusion

Entry of the amendments submitted with the preliminary amendment is requested at this time. Consideration of all of the pending claims is requested. Patentability of the

claims over the cited combination of references has been established. The case is now believed to be in condition for allowance.

The undersigned would welcome a telephone call if that would assist in resolving any issues remaining in the case.

Respectfully submitted,  
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